Please cancel Claims 5-7, 11, 12, and 16-18 without prejudice to applicants' right to pursue prosecution of these claims in a later-filed application.

REMARKS

Claims 1-18 were pending in the subject application. By this Amendment, applicants have amended claims 1, 2, 4, 8, 9 and 13-15 and cancelled claims 5-7, 11, 12 and 16-18 without prejudice to applicants' right to pursue prosecution of these claims in a later filed application. Accordingly, claims 1-4, 8-10 and 13-15 are presently under examination.

Applicants maintain that amended claims 1, 2, 4, 8, 9 and 13-15 do not involve the introduction of new matter. Claim 1 is supported in the specification at page 3, lines 34-37; claim 2 is supported at page 4, line 10 - page 5, line 5; claim 4 is supported at page 5, lines 6-14; claims 8 and 9 are supported at page 6, lines 22-36; and claims 13-15 are supported at page 7, line 26 to page 8, line 18. Accordingly, entry of amended claims 1, 2, 4, 8, 9 and 13-15 is respectfully requested.

In view of the foregoing amendments and the remarks which follow, applicants respectfully request that the Examiner reconsider and withdraw the various grounds of rejection set forth in the June 30, 1995 Office Action, and earnestly solicit allowance of the claims currently under examination, namely claims 1-4, 8-10

and 13-15.

Informalities

The objections on the Notice of Draftperson's Patent Drawing Review have been noted. Applicants will prepare and submit formal drawings upon the Examiner's allowance of the claims.

"Cobas-fara" has been changed to "Cobas-FARA" by amendment hereinabove, as suggested by the Examiner.

35 U.S.C. §112, First and Second Paragraph Objections and Rejections

The Examiner objected to the specification and rejected claims 1-18 under 35 U.S.C. §112, first paragraph. In this regard, the Examiner objected to Figure 2 because the axes and/or peaks were not labelled. Applicants respectfully traverse this objection to the specification and the rejection to the Claims.

The specification describes that Figure 2 represents a scan of adenylate kinase isoenzyme activities after electrophoretic resolution of a hemolyzed serum sample (see specification, page 3, lines 12-15). The specification further describes that the direction of migration is from cathode (represented by "-" on Figure 2) to anode (represented by "+" on Figure 2). Applicants submit that one skilled in the art reading Figure 2 would be able to understand and interpret the data presented therein with

reference to the specification. Applicants also submit that it is not customary in the art to label the axes on a representation of a scan of electrophoretically resolved isoenzyme activity as depicted in Figure 2 (see page 142, Journal of Clinical Laboratory Analysis, 8:140-143 (1994), submitted in IDS filed April 13, 1995). Therefore, amendment of Figure 2 is not required. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw the objection to the specification and the rejection to the claims under 35 U.S.C. §112, first paragraph.

The Examiner also rejected claims 1-18 under 35 U.S.C. §112, second paragraph, as indefinite for failing to particularly point out and distinctly claim the subject matter which applicants' regard as their invention.

In this regard, Examiner stated that claims 1 and 11 appear to be substantial duplicates. Applicants have cancelled claim 11 hereinabove. Accordingly, this rejection is moot.

The Examiner also stated that claims 1, 11 and 12 are inconsistent in reciting "detecting the presence of hemolyzed erythrocytes in blood", "diagnosing a hemolytic condition", and "monitoring the level of hemolysis in a subject being treated for hemolysis" in their respective preambles but failing to recite a positive corresponding method step and failing to correlate the detected erythrocyte adenylate kinase to such detection. Applicants have cancelled claims 11 and 12 hereinabove and amended

claim 1. Amended claim 1 recites a positive method step and correlates the detection of erythrocyte adenylate kinase to the presence of hemolyzed erythrocytes.

The Examiner also stated that claims 2-3 and 14-15 imply rather than positively state that a particular reagent system is required to provide a specific reaction product which can be measured by the explicitly required detection means. Claims 2, 14 and 15 have been amended to more particularly define the adenylate kinase-specific visualization reagent.

The Examiner also stated that "if present" in claim 2, line 2 is confusing. This language has been deleted from claim 2 by amendment hereinabove.

The Examiner also suggested inserting "said" before "erythrocyte" in claim 4, line 4 for proper antecedent basis. Applicants submit this is not necessary in view of the amendment to Claim 4 hereinabove.

In addition, the Examiner questioned "effected by" in claims 5-9. This rejection is moot since claims 5-7 have been cancelled and claims 8 and 9 have been amended to delete this language.

Finally, the Examiner rejected "a hemolytic condition" in claim 11. This rejection is moot in view of the cancellation of claim 11 hereinabove.

In view of the preceding amendments and remarks, applicants respectfully request that the Examiner reconsider and withdraw the rejection to the claims under 35 U.S.C. §112, second paragraph.

The Examiner also rejected claims 1-18 under 35 U.S.C. §112, first and second paragraphs, for not describing the invention in full, clear, concise and exact terms as to enable any person skilled in the art to make and use the same, and/or for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention.

In this regard, the Examiner stated that "activity" in claim 12 is indefinite, and suggested that this term be deleted. This rejection is moot in view of the cancellation of claim 12 hereinabove.

The Examiner also stated that claims 2, 14 and 15 are vague and indefinite in reciting "an adenylate kinase-specific visualization reagent". Claims 2, 14 and 15 have been amended hereinabove to more particularly define "adenylate kinase-specific visualization reagent."

The Examiner also stated that claims 8 and 9 are confusing in reciting "isotopic means" and "nonisotopic means". Claims 8 and 9 have been amended hereinabove by replacing the above terms with a radioactive and a non-radioactive label, respectively.

Finally, the Examiner rejected claim 11 as vague and indefinite for reciting "diagnosis of a hemolytic condition." This rejection is moot in view of the cancellation of claim 11 hereinabove.

In view of the preceding amendments and remarks, applicants respectfully request that the Examiner reconsider and withdraw the rejection to the claims under 35 U.S.C. §112, first and second paragraphs.

35 U.S.C. §103 Rejection

Claims 1-18 were rejected under 35 U.S.C. §103 as unpatentable over Mainzer, et al. and Henry in view of Le Gall, et al., Buth, et al., Kurokawa, et al. and Koyama, et al. Applicants respectfully traverse the above rejection, and maintain that the claimed invention is patentable over the references cited by the Examiner. None of the references cited by the Examiner, alone or in combination, taught or suggested the methods of the present invention.

Mainzer, et al. taught that free hemoglobin is a very sensitive indicator for intravascular hemolysis and MK, i.e. myokinase, will diagnose intramuscular diseases. Mainzer did not teach or suggest that the presence of hemolyzed erythrocytes in a serum sample may be detected by detecting erythrocyte adenylate kinase. Applicants note that myokinase is derived from muscle,

whereas erythrocyte adenylate kinase is derived from the erythrocyte and that both are different enzymes.

Henry described a general discussion of hemolysis and laboratory tests for its detection. Henry did not disclose the use of erythrocyte adenylate kinase in the detection of hemolyzed erythrocytes.

Le Gall, et al. described a general procedure for separating G-6-P dehydrogenase enzymes using cellulose acetate electrophoresis. Buth, et al. also described an improvement in a general enzyme-linked electrophoretic staining procedure. Neither Le Gall, et al. nor Buth, et al. taught or suggested a method of specifically detecting erythrocyte adenylate kinase.

Kurokawa, et al. described the use of a monoclonal antibody directed against crystallized porcine muscle AK_1 to detect human serum AK_1. Kurokawa, et al. also did not distinguish erythrocyte adenylate kinase from the other forms of adenylate kinase present in serum, i.e., that derived from other sources such as muscle and liver. Kurokawa, et al. did not teach or suggest a method for specifically detecting erythrocyte adenylate kinase.

Koyama, et al. described antibody cross reactivity between three fragments of porcine, muscle adenylate kinase. Koyama, et al. did not teach or suggest a method for specifically detecting erythrocyte adenylate kinase.

In summary, none of the references cited by the Examiner, either alone or in combination, taught or suggested the method of the present invention, i.e., a method for detecting the presence of hemolyzed erythrocytes in a serum sample by the detection of erythrocyte adenylate kinase.

In view of the preceding amendments and remarks, applicants respectfully request that the Examiner reconsider and withdraw the rejection to the claims under 35 U.S.C. §103.

If a telephone interview would further the prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone at the number provided below.

No fee, other than the $450.00 fee for a three month extension of time, is deemed necessary in connection with the filing of this Amendment. If any fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 01-1785.

"Express Mail" mailing label no. EM220934625US
Date of Deposit 1-2-96
I hereby certify that this paper or fee is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to the Commissioner of Patents and Trademarks, Washington, D.C. 20231
JEFFREY MENDEZ
Jeffrey Mendez
(Signature of person mailing paper or fee)

Dated: January 2, 1996
New York, New York

Respectfully Submitted,

AMSTER, ROTHSTEIN & EBENSTEIN
Attorneys for Applicants
90 Park Avenue
New York, New York 10016
(212) 697-5995

By Craig J. Arnold
Craig J. Arnold
Registration No. 34,287